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- (74) Agent: **MILLER, Raymond, A.**; Pepper Hamilton LLP, 500 Grant Street, One Mellon Center, 50th Floor, Pittsburgh, PA 15219 (US).
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- (71) Applicant (*for all designated States except US*): **NORTH-WESTERN UNIVERSITY** [US/US]; 1880 Oak Avenue, Suite 100, Evanston, IL 60201 (US).
- (72) Inventors; and
(75) Inventors/Applicants (*for US only*): **STUPP, Samuel, I.** [US/US]; 57 E. Delaware Place, Apartment 2802, Chicago, IL 60611 (US). **BENIASH, Elia** [IL/US]; 4615 Davis Street, Skokie, IL 60076 (US). **HARTGERINK, Jeffrey, D.** [US/US]; 1115 Elmwood Avenue, Evanston, IL 60202 (US).
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(54) Title: COMPOSITION AND METHOD FOR SELF-ASSEMBLY AND MINERALIZATION OF PEPTIDE AMPHIPHILES

(57) Abstract: The present invention is directed to a composition useful for making homogeneously mineralized self assembled peptide-amphiphile nanofibers and nanofiber gels. The composition is generally a solution comprised of a positively or negatively charged peptide-amphiphile and a like signed ion from the mineral. Mixing this solution with a second solution containing a dissolved counter-ion of the mineral and/or a second oppositely charged peptide amphiphile, results in the rapid self assembly of the peptide-amphiphiles into a nanofiber gel and templated mineralization of the ions. Templated mineralization of the initially dissolved mineral cations and anions in the mixture occurs with preferential orientation of the mineral crystals along the fiber surfaces within the nanofiber gel. One advantage of the present invention is that it results in homogenous growth of the mineral throughout the nanofiber gel. Another advantage of the present invention is that the nanofiber gel formation and mineralization reactions occur in a single mixing step and under substantially neutral or physiological pH conditions. These homogeneous nanostructured composite materials are useful for medical applications especially the regeneration of damaged bone in mammals. This invention is directed to the synthesis of peptide-amphiphiles with more than one amphiphilic moment and to supramolecular compositions comprised of such multi-dimensional peptide-amphiphiles. Supramolecular compositions can be formed by self assembly of multi-dimensional peptide-amphiphiles by mixing them with a solution comprising a monovalent cation.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/35902

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 38/16, 38/10, 38/08; C07K 7/08, 7/06, 14/16; G01N 33/53, 33/554, 33/543.
US CL : 514/12, 13, 14, 15, 16; 530/324, 326, 327, 328, 332, 350, 402; 436/518, 519, 524, 527.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : A61K 38/16, 38/10, 38/08; C07K 7/08, 7/06, 14/16; G01N 33/53, 33/554, 33/543.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO WEST (Examiner search tool) and Medline.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ISSAC, R. et al. Approaching exponential growth with a self-replicating peptide. J. Am. Chem. Soc. January 2002, Vol. 124, pages 6808-6809. The entire document.	1-11
X	HARTGERINK, J.D. et al. Peptide-amphiphile nanofibers: a versatile scaffold for the preparation of self-assembling materials. Proc. Natl. Acad. Sci. U S A. April 2002, Vol. 99, pages 5133-5138. The entire document.	1-3 and 9-10
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Y		
X	SANTOSO, S. S. et al. Solute equilibration curves, crossing time for urea and glucose during peritoneal dialysis: a function of age in children.	1-3 and 9-11
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Y		
Y	STEPHANIE, F. B. et al. Progress toward a peptidomimetic of laminin-derived pentapeptide YIGSR: synthesis of the unique tricyclic core structure. J. Org. Chem. August 2002, Vol. 67, pages 6097-6103. The entire document.	1-3 and 9-11.
X,P	NIECE, K. L. et al. Self-assembly combining two bioactive peptide-amphiphile molecules into nanofibers by electrostatic attraction.	1-3 and 9-11
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Y,P	J. Am Chem Soc. June 2003, Vol. 125, pages 7146-7147. The entire document.	

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

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Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Samuel W Liu

Telephone No. 703-306-3441

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HARTGERINK, J. D. et al. Self-assembly and mineralization of peptide-amphiphile nanofibers. Science. November 2001, Vol. 294, pages 1684-1688. The entire document.	1-3
X,P	ZHANG, S. Fabrication of novel biomaterials through molecular self-assembly. Nat. Biotechnol. October 2003, Vol. 21, pages 1171-1178. The entire document.	9-10
X,P	US 2003/0176335 A1 (ZHANG, S.) 18 September 2003, Abstract, columns [0008], [0015]-[0032], Tables 2-4, and claims 1-40.	1-11